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Original Article

Screening frequency and histologic type influence the efficacy of cervical cancer screening: A nationwide cohort study

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ABSTRACT

Objective: To evaluate the influence of age, screening interval, and histologic type on the effect of Pap smears in cervical cancer screening.

Materials and methods: Data were retrieved from the Taiwan National Cancer Registry and Cervical Cancer Screening Registration System for the period from 2002 to 2010. Age, Pap smear interval, FIGO stage, and histology were further analyzed.

Results: A total of 12,294 women with cervical cancer were enrolled, including 10,040 with squamous cell carcinoma (SCC), 1720 with adenocarcinoma (ADC), 401 with adenosquamous carcinoma (ASC), and 133 with small cell neuroendocrine carcinoma (SMC). Women who had a Pap smear at an interval of <3 years had a significantly higher proportion of stage I disease than women who had never undergone cervical cancer screening ($p < 0.0001$). Greater than 40% of women with SCCs in each age group had never had a Pap smear; however, women with ADCs were predominantly in the younger age and greater than 40% of women with ADCs had Pap smear at intervals < 3 years.

Conclusions: Pap smear is more effective in screening for cervical SCCs compared to cervical ADCs. Improving adherence to screening recommendations is important for the prevention of cervical SCC, especially in elderly women.

Introduction

Cervical cancer is a major cause of mortality and morbidity among women worldwide, including Taiwan. The incidence of cervical cancer has decreased significantly with the introduction of Pap smear screening programs in many countries; however, it remains a major issue among women living in less developed countries. Human papillomavirus (HPV) is regarded to be the cause of cervical cancer [1]. A combination of HPV testing and Pap smear is currently considered the optimal method for detecting cervical lesions [2]. Indeed, Pap smear remains the most simple and important screening tool for cervical cancer in most parts of the world, especially in regions with limited resources [3]. The factors required to successfully implement Pap screening include a comprehensive screening program, adequate training of providers, and adherence to the screening program [4–10]. Pap smear can decrease the incidence of cervical cancer (mainly squamous cell carcinoma) in many parts of the world [3,6,11–16]; however, the incidence of cervical adenocarcinoma has not shown the same decreasing trend. An increase in the incidence of adenocarcinoma

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has been reported in the US [12], Canada [13], and the Asia-Pacific region [6].

In the present study, data on Pap smear from women with invasive cervical cancer were retrieved from the Taiwan National Cancer Registry and Taiwan Cervical Cancer Screening Registration System. The aim of this study was to analyze the relationships between age, Pap smear history, and Pap smear results in women with primary invasive cervical cancer.

Materials and methods

The National Taiwan Cancer Registry was implemented in 1979 [17]. The information in the system is processed according to the standard guidelines of the International Agency for Research on Cancer (IARC). The disease codes are based on the International Classification of Diseases for Oncology, Third Edition (ICD-O-3), and the histologic types are classified according to the World Health Organization Classification of Tumors [18]. A total of 214 hospitals with >50 beds are mandated to report cancer cases to the Taiwan Cancer Registry. The quality of the Taiwan Cancer Registry database has been excellent after enactment of the Cancer Control Act in 2003 [19]. The morphologic verification (MV% [the proportion of incident cases with histologic and/or cytologic verification of a cancer diagnosis]) increased from 87.4% in 2002 to 91.3% in 2011. The rate of death certificates only (DCO% [the proportion of incident cases with information based on death certificates only]) decreased from 2.9% in 2002 to 0.8% in 2011. The MV% and DCO% for cervical cancer were 99.6% and 0.3%, respectively, in 2011. Because the MV% and DCO% are complete and of high quality, the database is regarded as an important resource for academic research and establishment of cancer control policy in Taiwan [19].

An annual cervical screening program using the Pap smear was launched in Taiwan for women ≥30 years in 1995. Registered data include age, date of diagnosis, histologic diagnosis, and treatment. Cervical Pap smears were performed by gynecologists, family physicians, and trained public health nurses. Approximately 100 cytologic laboratories with cytologists or cytotechnicians performed the cytologic examinations of the Pap smears, and the results were further confirmed by certified cytopathologists. All Pap smears were revised according to the 2001 Bethesda system [20].

The research protocol was approved by the Ethics Committee of the National Taiwan University Hospital. Women diagnosed with a primary cancer of the cervix (ICD-O-3 C53) were eligible for this study. The data of women diagnosed with invasive cervical cancer from 1 January 2002 to 31 December 2010 were retrieved from the Taiwan National Cancer Registry, and individual Pap smear results were retrieved from the Taiwan Cervical Cancer Screening Registration System from 1 January 1995 to 31 December 2010. Staging of cervical cancer was based on the criteria of the International Federation of Gynecology and Obstetrics (FIGO staging) [21]. Four major histologic types, including squamous cell carcinoma (histologic codes 8050, 8051, 8052, 8070, 8071, 8072, 8073, 8074, 8075, 8076, 8077, 8082, 8094, and 8130), adenocarcinoma (histologic codes 8140, 8143, 8144, 8255, 8260, 8262, 8263, 8323, 8380, 8384, 8441, 8461, 8470, 8480, 8482, 8500, and 8570), adenosquamous carcinoma (histologic code 8560), and small cell neuroendocrine carcinoma (histologic codes: 8041, 8042, 8043, 8044, and 8045) were recruited. Mixed type tumors, sarcomas, melanomas, undefined tumor types, and other rare histologic types were excluded in the current study. Although an annual Pap screening program has existed in Taiwan for years, women undergo Pap screening voluntarily. Thus, the Pap smear interval was defined as the average time between Pap smears from the earliest Pap smear to the diagnosis of cervical cancer.

Statistical analysis

All data were analyzed using SAS software (version 9.1; SAS, Inc., Cary, NC). Comparisons between unpaired groups were made using a chi-square test for categorical variables. Age-standardized rates were calculated using the direct method with the world standard population in 2000, as defined by the World Health Organization, and expressed as cases per 100,000 population. Trends in the age-standardized rates were analyzed using the annual percent change by joinpoint regression analysis (Joinpoint Regression Program, version 3.5 [April 2011]; National Cancer Institute, Bethesda, MD) [22]. The best fitting trend lines where the rate changed significantly were chosen by Monte Carlo permutation tests. To quantify the trend in incidence, the average annual percentage change (AAPC) was estimated for four histologic types of invasive cervical cancer for women ≥ 30 years of age between 2002 and 2010. All statistical tests were two-tailed, and a p value < 0.05 was considered statistically significant.

Results

There were 554 women excluded from the study for undefined or rare histological types. A total of 12,294 women with invasive cervical carcinoma were finally enrolled in this study (Table 1), including 10,040 women with squamous cell carcinoma (SCC), 1720 women with adenocarcinoma (ADC), 401 women with adenosquamous carcinoma (ASC), and 133 women with small cell neuroendocrine carcinoma (SMC). With respect to age, 1177 women were 30–39 years of age, 3135 women were 40–49 years of age, 3190 women were 50–59 years of age, 2196 women were 60–69 years of age, and 2596 women were ≥70 years of age. Overall, 6666 women had FIGO stage I disease, 3439 women had FIGO stage II disease, 1332 women had FIGO stage III disease, and 857 women had FIGO stage IV disease. With respect to Pap smear interval, 3106 women had a Pap smear interval <3 years, 1333 women had a Pap smear interval between 3 and 5 years, 2070 women had a Pap smear interval >5 years, and 5785 women had never had a Pap smear.

The incidence of cervical cancer decreased especially for squamous cell carcinoma

As shown in Fig. 1A, the standardized incidence rate of cervical cancer decreased from 2002 (SCC: 27.83, ADC: 4.32, ASC: 0.95, SMC:

Table 1
Characteristics of 12,294 women with cervical cancer.

	SCC[a]	%	ADC[a]		ASC[a]	%	SMC[a]	%	Total
	N		N	%	N		N		N
Age									
30–39	859	8.6	249	14.5	46	11.5	23	17.3	1177
40–49	2335	23.3	612	35.6	142	35.4	46	34.6	3135
50–59	2571	25.6	464	27.0	128	31.9	27	20.3	3190
60–69	1925	19.2	215	12.5	40	10.0	16	12.0	2196
70–	2350	23.4	180	10.5	45	11.2	21	15.8	2596
FIGO stage									
I	5166	51.5	1161	67.5	276	68.8	63	47.4	6666
II	2997	29.9	333	19.4	77	19.2	32	24.1	3439
III	1188	11.8	100	5.8	24	6.0	20	15.0	1332
IV	689	6.9	126	7.3	24	6.0	18	13.5	857
Pap screening interval									
<3 years	2174	21.7	759	44.1	133	33.2	40	30.1	3106
3–5 years	1040	10.4	228	13.3	49	12.2	16	12.0	1333
>5 years	1724	17.2	275	16.0	54	13.5	17	12.8	2070
Never	5102	50.8	458	26.6	165	41.1	60	45.1	5785
Total	10,040		1720		401		133		12,294

[a] SCC: squamous cell carcinoma, ADC: adenocarcinoma, ASC: adenosquamous carcinoma, SMC: small cell neuroendocrine carcinoma, FIGO: International Federation of Gynecology and Obstetrics.

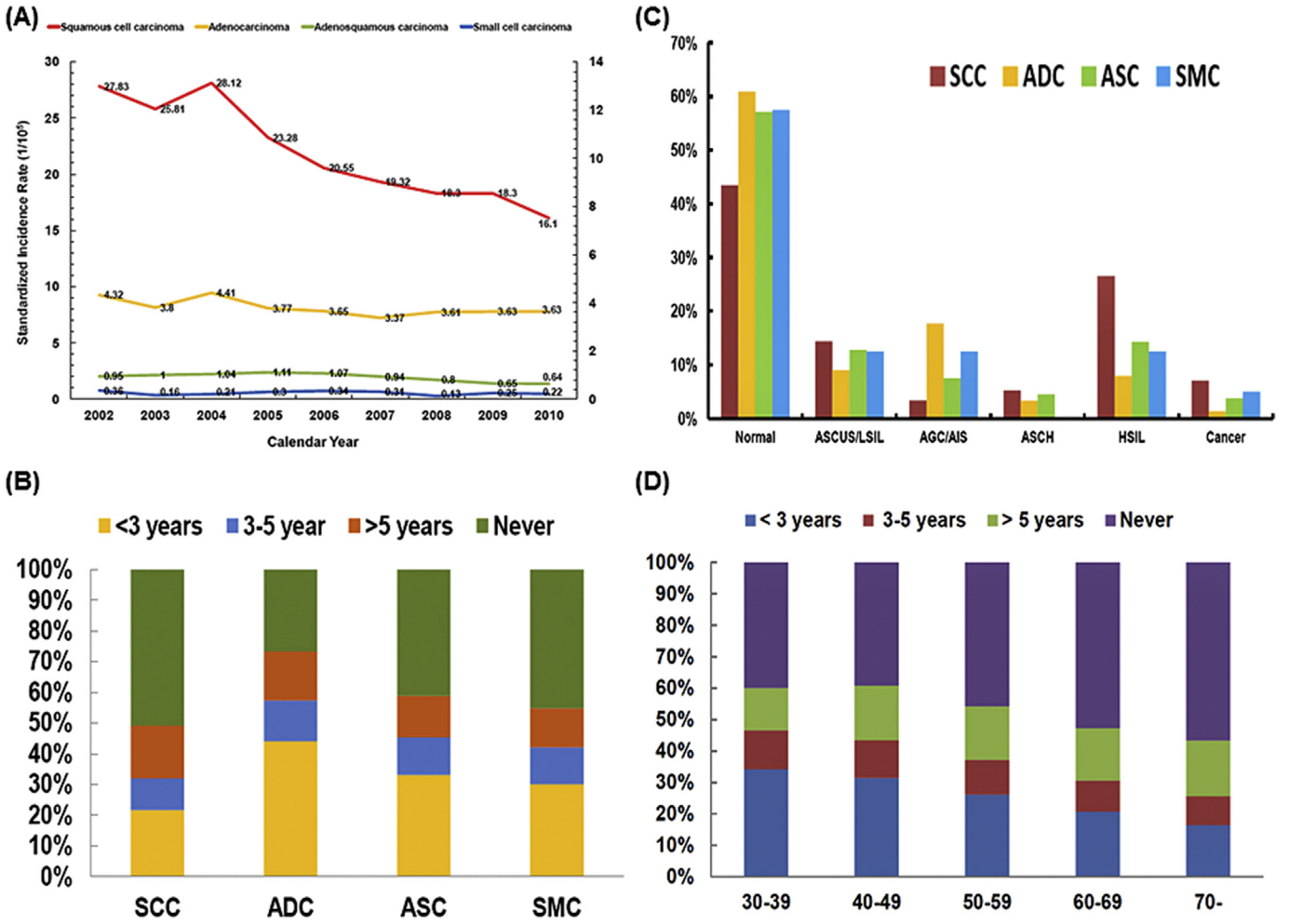

Fig. 1. **(A)** The standardized incidence for various histologic types of cervical cancer in Taiwan from 2002 to 2010. The left side of the Y-axis is the incidence of SCC, and the right side of the Y-axis shows the incidences of ADC, ASC, and SMC. *Note:* The incidence of cervical cancer generally decreased, especially for SCC. **(B)** The distribution of Pap smear intervals amongst the various histologic types. *Note:* Greater than one-half of the women with SCCs never received a Pap smear; however, only approximately one-fourth of the women with ADCs never had a Pap smear. **(C)** The most advanced Pap smear results occurred in the women with a Pap smear interval < 3 years amongst the different histologic types. *Note:* Compared with SCC, the rates of normal Pap smear results were significantly higher in the women with ADCs, ASCs, and SMCs. **(D)** The distribution of Pap smear intervals in the various age groups. *Note:* Greater than one-half of the women > 70 years of age never had a Pap smear.

0.36 in 100,000 women) to 2010 (SCC: 16.1, ADC: 3.62, ASC: 0.64, SMC: 0.22 in 100,000 women). Trends in age-standardized rates analyzed by joinpoint regression analysis showed a significant decrease in the AAPC for SCC (−6.8%, 95% confidence interval (CI): −8.6% ~ −5.0%), ADC (−2.3%, 95% CI: −4.2% ~ −0.3%), and ASC (−5.8%, 95% CI: −8.4% ~ −3.0%). The AAPC was −5.0% (95% CI: −13.9%–4.7%) for SMC which did not reach statistical significance.

Different distribution of the Pap-attending intervals among women with primary cervical cancer

The distribution of the Pap-attending intervals among the histological types was significantly different (chi-square test, $p < 0.0001$). Of the women with SCC, 21.7% had an interval of <3 years, but 50.8% of them had never received a Pap smear (Fig. 1B). Of the women with ADC, ASC and SMC, were 44.1%, 33.2% and 30.1%, had a Pap smear interval <3 years, respectively. Only, 26.6% of the ADC women, 41.1% of the ASC women and 45.1% of the SMC women had never had a Pap smear.

The distribution of the Pap smear intervals among the age groups was significantly different (chi-square test, $p < 0.0001$). Of the women 30–39, 40–49, 50–59, 60–69, and ≥70 years of age, 34.2%, 31.5%, 26.1%, 20.7% and 16.4%, had a Pap smear interval <3 years, respectively (Fig. 1D). However, 39.9% of the 30–39 year old women, 39.2% of the 40–49 year old women, 45.8% of the 50–59 year old women, 52.7% of the 60–69 year old women, and 56.6% of the ≥70 year old women had never had a Pap smear.

The women with ADCs, ASCs, and SMCs had higher false-negative screening results than women with SCCs

The most severe Pap smear results of women with cervical cancer who had a Pap smear interval <3 years were further evaluated (Fig. 1C). A high-grade squamous intraepithelial lesion (HSIL) was the most frequent abnormal Pap smear result in women with SCCs (26.5%) and ASCs (14.3%); however, atypical glandular cells/adenocarcinoma *in situ* (AGC/AIS) was the most frequent abnormal Pap smear result in women with ADCs (17.7%). No dominant abnormal Pap smear result was noted in the SMC group. Compared with women who had SCCs (43.4%), women with ADCs (60.9%), ASCs (57.1%), and SMCs (57.5%) had higher proportions of normal Pap smear results ($p < 0.0001$ [chi-square test]).

Women with ADCs and ASCs had higher proportions of FIGO stage I disease than women with SCCs regardless of the previous Pap smear screening history

With respect to FIGO stage, 51.5% of the women with SCCs were stage I, 29.9% were stage II, 11.8% were stage III, and 6.9% were stage IV (Fig. 2A) compared to 67.5%, 19.4%, 5.8%, and 7.3% of women with ADCs, respectively. Of women with ASCs, 68.8% were FIGO stage I, 19.2% were stage II, 6.0% were stage III, and 6.0% were stage IV. Of women with SCCs who had never had a Pap smear, 42.5% were stage I, 34.3% were stage II, 14.4% were stage III, and 8.8% were stage IV compared to 52.8%, 26.4%, 9.2%, and 11.6% of women with ADCs who had never had a Pap smear, respectively (Fig. 2B). The proportions of FIGO stage I disease in the women with SCCs and SMCs who had never had a Pap smear were significantly lower than women with ADCs and ASCs ($p < 0.0001$ [chi-square test]). Women with ADCs (73.5%) and ASCs (76.7%) who had Pap smear at < 3-year intervals had higher proportions of early-stage disease (FIGO stage I) than women with SCCs (66.1%) and SMCs (50%), as shown in Fig. 2C (<0.0001 [chi-square test]). In addition, women with SCCs, ADCs, and ASCs who had a Pap smear interval <3 years had significantly higher proportions of stage I disease than women who had never had a Pap smear ($p < 0.0001$ [chi-square test]).

Proportion of women with SCCs increased gradually with age, but decreased in women with ADCs

The distribution of the various histologic types of cervical cancer among the different age groups was significantly different (Fig. 3A; $p < 0.0001$ [chi-square test]). Greater than 70% of the women with cervical cancer had SCC independent of age. The proportion of women with SCCs increased gradually with age (72.9% [30–39 years], 74.5% [40–49 years], 80.6% [50–59 years], 87.7% [60–69 years], and 90.5% [≥70 years]; $p < 0.0001$ [chi-square test]). A similar trend was also observed in the women with cervical cancer women who had never had a Pap smear (Fig. 3B; $p < 0.0001$ [chi-square test]) and women who had a Pap smear with an interval < 3 years (Fig. 3C; $p < 0.0001$ [chi-square test]). In contrast, the proportions of women with ADCs decreased gradually with age (Fig. 3A; 21.2% [30–39 years], 19.5% [40–49 years], 14.5% [50–59 years], 9.8% [60–69 years]; $p < 0.0001$ [chi-square test]). Women who had never had a Pap smear (Fig. 3B; $p < 0.0001$ [chi-square test]) and who had a Pap smear at an interval < 3 years (Fig. 3C; $p < 0.0001$ [chi-square test]) had similar trends.

A greater proportion of women with ADCs had frequent Pap smears than women with SCCs

Amongst women with SCCs 30–39 years of age, 30.8% had a Pap smear interval < 3 years, but 44.2% had never had a Pap smear (Fig. 4A). Of the women with SCCs 40–49, 50–59, 60–69, and ≥70 years of age, 26.8%, 22.8%, 17.8%, and 15.1% had Pap smears at an interval <3 years, respectively. Amongst women with ADCs 30–39 years of age, 47.8% had a Pap smear interval < 3 years, but 24.9% had never had a Pap smear (Fig. 4B). Of the women with ADCs 40–49, 50–59, 60–69, and ≥70 years of age, 46.9%, 44.2%, 43.3%, and 30.6% had a Pap smear interval < 3 years, respectively.

Among women with ASCs 30–39, 40–49, 50–59, 60–69, and ≥70 years of age, 30.4%, 40.8%, 28.1%, 37.5%, and 22.2% had a Pap smear interval <3 years, respectively (Fig. 4C). Among women with SMCs 30–39, 40–49, 50–59, 60–69, and ≥70 years, 21.7%, 37.0%, 22.2%, 31.3%, and 33.3% had a Pap smear interval <3 years, respectively (Fig. 4D). Greater than 40% of women with SCCs in each age group had never had a Pap smear, but >40% of women with ADCs in each age group (except the ≥70-year-old group) had a Pap smear interval < 3 years.

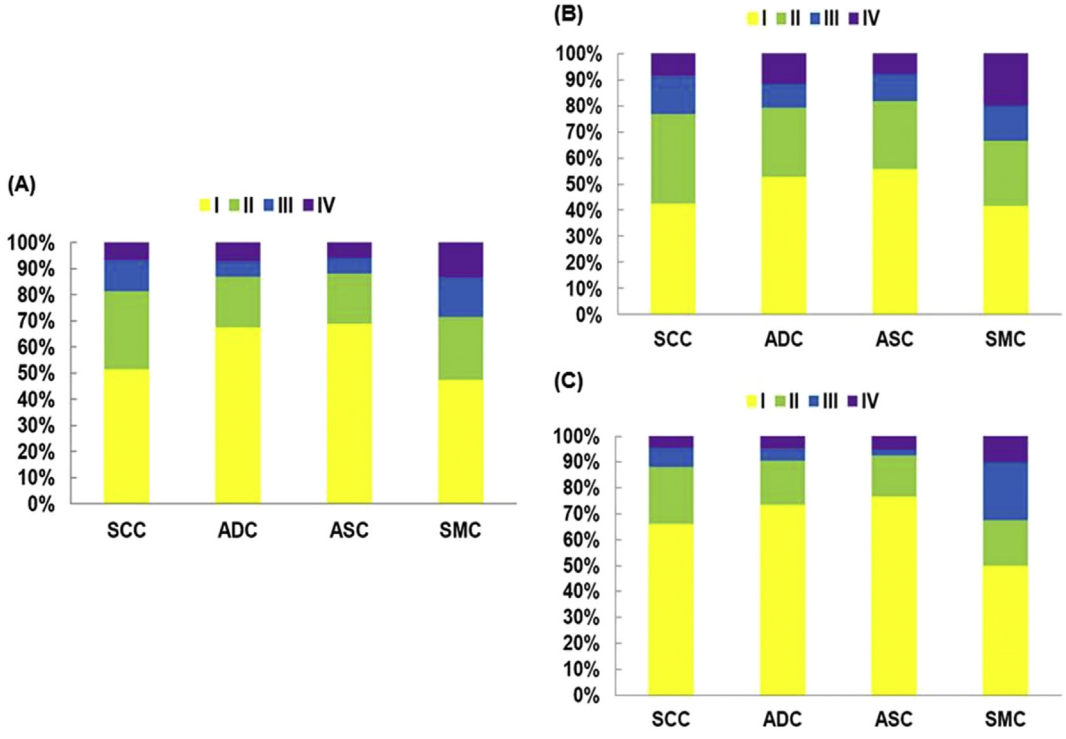

Fig. 2. **(A)** The FIGO stages of cervical cancers amongst the various histologic types. **(B)** The FIGO stages of the women who never had a Pap smear before diagnosis. **(C)** The FIGO stages of the women who had Pap screening at an interval < 3 years before diagnosis. *Note:* The women who had a short Pap smear interval had more stage I disease than women who had never had a Pap smear, except for the SMC group. The women with ADCs and ASCs had higher rates of stage I disease than the women with SCCs, regardless of the Pap smear screening history.

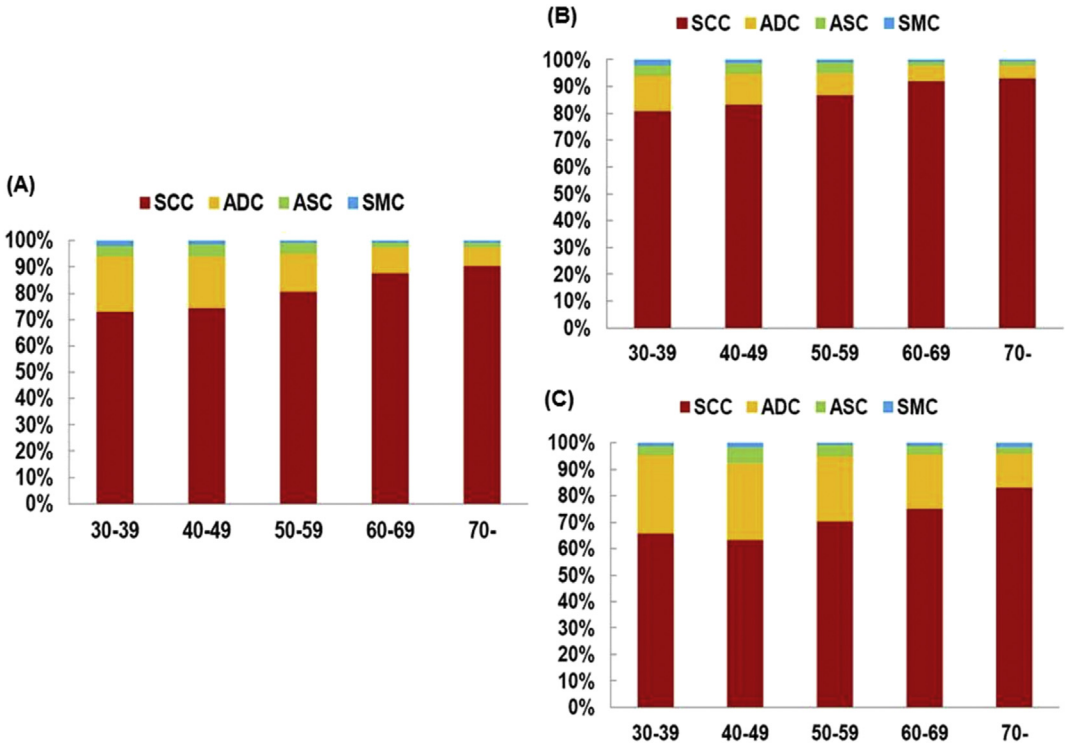

Fig. 3. **(A)** The distribution of various histologic types amongst different age groups for all women with cervical cancer. **(B)** The distribution of various histologic types amongst different age groups for the women who never had a Pap smear. **(C)** The distribution of histologic types amongst different age groups for the women with a Pap smear interval < 3 years before diagnosis. *Note:* SCC was the predominant histologic type amongst all age groups. The rate of SCC increased, but the rate of ADC decreased as women aged, regardless of the Pap smear screening history.

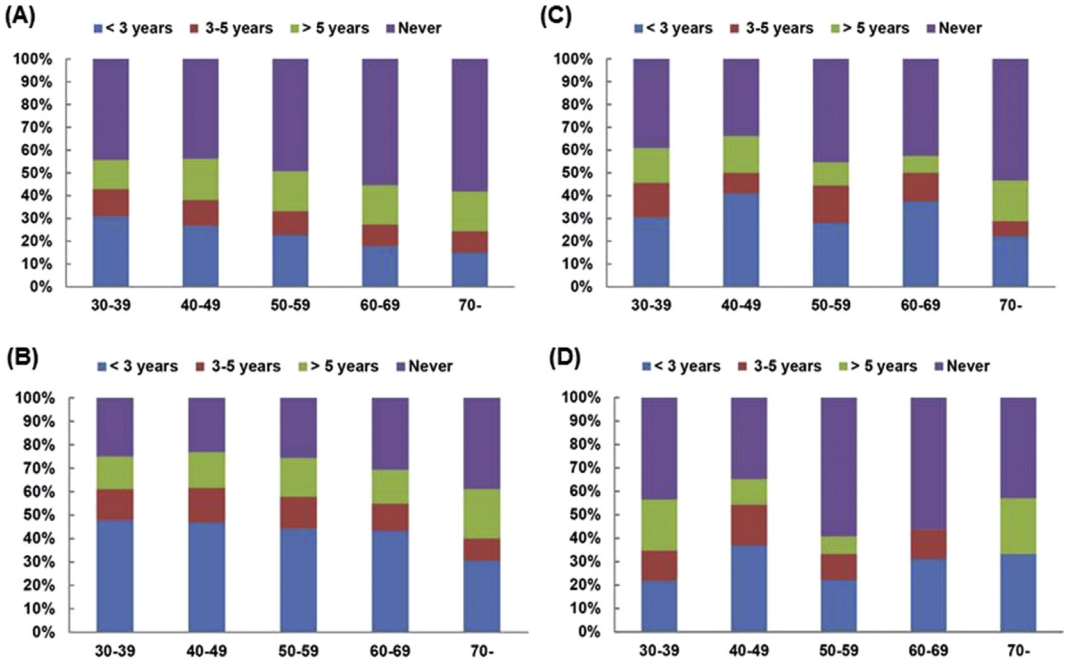

Fig. 4. **(A)** The distribution of Pap smear intervals amongst different age groups of women with SCC. **(B)** The distribution of Pap smear intervals amongst different age groups of women with ADC. *(C)* The distribution of Pap smear intervals amongst different age groups of women with ASC. **(D)** The distribution of Pap smear intervals amongst different age groups of women with SMCs. *Note:* Greater than 40% women with SCCs had never had a Pap smear, but >40% women with ADCs had a Pap smear interval < 3 years.

Discussion

The current study has provided a nationwide survey of Pap smear histories in women with cervical cancer. In Taiwan, a nationwide cervical cancer screening program initiated in 1995 provided an opportunity for annual Pap screening for every woman [23]; however, Taiwanese women undergo Pap smear screening voluntarily, therefore our study only revealed the relationship between Pap smear screening history and cervical cancer. The main limitation of this study was the retrospective design. Despite the

retrospective design, we are of the opinion that our findings still provide clinicians with useful information.

The benefits of using Pap smears to decrease the incidence and burden of cervical cancer have been reported. The SEER database showed that the overall incidence of cervical cancer decreased by 54% in the US over a 35-year period [12]. Canadian Pap screening programs involving an early age of initiation and frequent Pap smear intervals were established in the 1970s, and have resulted in a decreased incidence and mortality of cervical cancer [13]. Well-organized screening programs have also been shown to be highly effective in reducing the incidence of cervical SCC in Europe [14]. Over the last few decades, there has been a marked decrease in the incidence of cervical cancer across most areas of the Asia-Pacific region [6]. A lack of effective screening programs has been reported to be a major reason for the low rate of success in preventing cervical cancer [4,5]. Indeed, a comprehensive screening network system and adequate training of healthcare personnel are necessary for a Pap smear screening program [6–8].

Many women with cervical cancer, and especially women with SCCs, had never had a Pap smear based on the current study. A Danish study revealed that >45% of women with cervical cancer had inadequate cervical cancer screening [24]. In Malaysia, many women with cervical cancer had not had a Pap smear within 3 years preceding the diagnosis of cervical cancer [25]. The incidence and mortality of cervical cancer has been reported to decrease significantly in women with an increased frequency of Pap smears compared to women who have never had a Pap smear [26]. In Thailand, women who have been screened multiple times are at substantially lower risk for cervical cancer than women who are only screened a few times [27]. Indeed, improving the frequency of screening, quality, and cost of Pap smear screening is important and cost-effective [7,27–30]. The factors affecting adherence to cervical cancer screening includes a lack of knowledge of the disease, insurance coverage, socioeconomic status, heritage acculturation, religious barriers, and psychosocial issues [6–10]. In spite of a well-organized public cervical screening program, correct education to healthcare providers and the population are necessary for the success of cervical cancer prevention [8]. Thus, further education regarding Pap smear screening and cervical cancer is important for the general population, especially in women who have never had a Pap smear, and low-income or at-risk groups [31,32].

Our study showed that women with ADC were younger and had a regular Pap smear screening history. The Pap smear alone is not effective for the prevention and early detection of cervical ADC. The incidence of cervical ADC has not shown the same decreasing trend as SCC in Taiwan [11]. The SEER database showed that the incidence of ADC increased by 32.2% in spite of an overall decrease in the incidence of invasive cervical cancer [12]. An increasing trend of cervical ADC has also been reported in Europe [33] and the Asia-Pacific region [6]. Our results showed that younger women with ADCs generally had more frequent Pap screening, although such women had higher false-negative screening results than women with SCCs. Chen et al. [26] also reported that the Pap smear did not reduce the risk of ADC as much as SCC. For women who attended near-annual screening, the hazard ratios of the incidence and mortality of SCC were 0.18 and 0.09, respectively, and 0.66 and 0.56 in women with ADC, respectively [26]. Thus, a cytologic screening procedure alone is not an effective method to prevent cervical ADC, and further effective methods for the screening and prevention of cervical ADC and ASC are needed.

Cervical ADCs are more common in younger women and have a negative impact on survival [34]. The prevalence of HPV infections in women with ADCs and ASCs are 36.2% for HPV 16 and 51.5% for HPV 18 in Taiwanese women [31]. HPV 18 has been reported to be the most common type in women with ADCs and ASCs, in contrast to HPV 16 in women with SCCs [32,35,36]. HPV testing and vaccination could be helpful in reducing the incidence of cervical cancer in younger women, and especially ADCs and ASCs. A 5-year Pap smear interval for women ≥30 years of age with a “double-negative” Pap smear and high-risk HPV results has been suggested [2,37]. In combination with cytology, HPV DNA testing is the preferred method for cervical screening [38,39]. Using HPV testing alone or incorporating HPV testing with cytology would be helpful for the earlier identification of cervical ADC [40].

Conflicts of interest

The authors declare that they have no conflicts of interest.

References

[1] zur Hausen H. Papillomaviruses and cancer: from basic studies to clinical application. Nat Rev Cancer 2002;2(5):342–50.
[2] Dinkelspiel H, Kinney W. State of the science: cervical cancer screening in transition. Gynecol Oncol 2014;133(3):389–93.
[3] Seol HJ, Ki KD, Lee JM. Epidemiologic characteristics of cervical cancer in Korean women. J Gynecol Oncol 2014;25(1):70–4.
[4] Rogovskaya SI, Shabalova IP, Mikheeva IV, Minkina GN, Podzolkova NM, Shipulina OY, et al. Human papillomavirus prevalence and type-distribution, cervical cancer screening practices and current status of vaccination implementation in Russian Federation, the Western countries of the former Soviet Union, Caucasus region and Central Asia. Vaccine 2013;31(Suppl 7):H46–58.
[5] Bray F, Lortet-Tieulent J, Znaor A, Brotons M, Poljak M, Arbyn M. Patterns and trends in human papillomavirus-related diseases in Central and Eastern Europe and Central Asia. Vaccine 2013;31(Suppl 7):H32–45.
[6] Moore MA, Tajima K. Cervical cancer in the asian pacific-epidemiology, screening and treatment. Asian Pac J Cancer Prev 2004;5(4):349–61.
[7] Woo JS, Brotto LA, Gorzalka BB. The role of sexuality in cervical cancer screening among Chinese women. Health Psychol: Off J Div Health Psychol Am Psychol Assoc 2009;28(5):598–604.
[8] Ackerson K, Gretebeck K. Factors influencing cancer screening practices of underserved women. J Am Acad Nurse Pract 2007;19(11):591–601.
[9] Sancho-Garnier H, Khazraji YC, Cherif MH, Mahnane A, Hsairi M, El Shalakamy A, et al. Overview of cervical cancer screening practices in the extended Middle East and North Africa countries. Vaccine 2013;31(Suppl 6):G51–7.
[10] Park MJ, Park EC, Choi KS, Jun JK, Lee HY. Sociodemographic gradients in breast and cervical cancer screening in Korea: the Korean National Cancer Screening Survey (KNCSS) 2005–2009. BMC Cancer 2011;11:257.
[11] Chen YY, You SL, Chen CA, Shih LY, Koong SL, Chao KY, et al. Effectiveness of national cervical cancer screening programme in Taiwan: 12-year experiences. Br J Cancer 2009;101(1):174–7.
[12] Adegoke O, Kulasingam S, Virnig B. Cervical cancer trends in the United States: a 35-year population-based analysis. J Womens Health (Larchmt) 2012;21(10):1031–7.
[13] Dickinson JA, Stankiewicz A, Popadiuk C, Pogany L, Onysko J, Miller AB. Reduced cervical cancer incidence and mortality in Canada: national data from 1932 to 2006. BMC Public Health 2012;12:992.
[14] Bray F, Loos AH, McCarron P, Weiderpass E, Arbyn M, Moller H, et al. Trends in cervical squamous cell carcinoma incidence in 13 European countries: changing risk and the effects of screening. Cancer Epidemiol Biomark Prev 2005;14(3):677–86.
[15] Sobue T, Suzuki T, Hashimoto S, Yokoi N, Fujimoto I. A case-control study of the effectiveness of cervical cancer screening in Osaka, Japan. Jpn J Cancer Res 1988;79(12):1269–75.
[16] Bray F, Loos AH, Tognazzo S, La Vecchia C. Ovarian cancer in Europe: cross-sectional trends in incidence and mortality in 28 countries, 1953–2000. Int J Cancer 2005;113(6):977–90.
[17] Registry TNC. Taiwan National Cancer Registry. http://tcrcphntuedutw/mainphp?Page=A1.
[18] Tavassoéli FA, Devilee P, World Health Organization Classification of Tumours. Pathology and genetics of tumours of the breast and female genital organs. Lyon: IARC Press; 2003.
[19] Chiang CJ, You SL, Chen CJ, Yang YW, Lo WC, Lai MS. Quality assessment and improvement of nationwide cancer registration system in Taiwan: a review. Jpn J Clin Oncol 2015;45(3):291–6.
[20] Solomon D, Davey D, Kurman R, Moriarty A, O'Connor D, Prey M, et al. The 2001 Bethesda System: terminology for reporting results of cervical cytology. JAMA 2002;287(16):2114–9.
[21] Pecorelli S. Revised FIGO staging for carcinoma of the vulva, cervix, and endometrium. Int J Gynaecol Obstet 2009;105(2):103–4.
[22] Kim HJ, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joinpoint regression with applications to cancer rates. Stat Med 2000;19(3):335–51.
[23] Chen CJ, You SL, Lin LH, Hsu WL, Yang YW. Cancer epidemiology and control in Taiwan: a brief review. Jpn J Clin Oncol 2002;32(Suppl):S66–81.

[24] Kirschner B, Poll S, Rygaard C, Wahlin A, Junge J. Screening history in women with cervical cancer in a Danish population-based screening program. Gynecol Oncol 2011;120(1):68–72.
[25] Othman NH, Devi BC, Halimah Y. Cervical cancer screening: patients understanding in major hospitals in Malaysia. Asian Pac J Cancer Prev 2009;10(4):569–74.
[26] Chen YY, You SL, Koong SL, Liu J, Chen CA, Chen CJ. Screening frequency and atypical cells and the prediction of cervical cancer risk. Obstet Gynecol 2014;123(5):1003–11.
[27] Kasinpila C, Promthet S, Vatanasapt P, Sasieni P, Parkin DM. Evaluation of the nationwide cervical screening programme in Thailand: a case-control study. J Med Screen 2011;18(3):147–53.
[28] Praditsitthikorn N, Teerawattananon Y, Tantivess S, Limwattananon S, Riewpaiboon A, Chichareon S, et al. Economic evaluation of policy options for prevention and control of cervical cancer in Thailand. PharmacoEconomics 2011;29(9):781–806.
[29] Lonnberg S, Nieminen P, Luostarinen T, Anttila A. Mortality audit of the Finnish cervical cancer screening program. Int J Cancer 2013;132(9):2134–40.
[30] Thippeveeranna C, Mohan SS, Singh LR, Singh NN. Knowledge, attitude and practice of the pap smear as a screening procedure among nurses in a tertiary hospital in north eastern India. Asian Pac J Cancer Prev 2013;14(2):849–52.
[31] Lai CH, Chou HH, Chang CJ, Wang CC, Hsueh S, Huang YT, et al. Clinical implications of human papillomavirus genotype in cervical adeno-adenosquamous carcinoma. Eur J Cancer 2013;49(3):633–41.
[32] Chen TM, Chen CA, Wu CC, Huang SC, Chang CF, Hsieh CY. The genotypes and prognostic significance of human papillomaviruses in cervical cancer. Int J Cancer 1994;57(2):181–4.
[33] Bray F, Carstensen B, Moller H, Zappa M, Zakelj MP, Lawrence G, et al. Incidence trends of adenocarcinoma of the cervix in 13 European countries. Cancer Epidemiol Biomark Prev 2005;14(9):2191–9.
[34] Galic V, Herzog TJ, Lewin SN, Neugut AI, Burke WM, Lu YS, et al. Prognostic significance of adenocarcinoma histology in women with cervical cancer. Gynecol Oncol 2012;125(2):287–91.
[35] Tase T, Okagaki T, Clark BA, Manias DA, Ostrow RS, Twiggs LB, et al. Human papillomavirus types and localization in adenocarcinoma and adenosquamous carcinoma of the uterine cervix: a study by in situ DNA hybridization. Cancer Res 1988;48(4):993–8.
[36] Castellsague X, Diaz M, de Sanjose S, Munoz N, Herrero R, Franceschi S, et al. Worldwide human papillomavirus etiology of cervical adenocarcinoma and its cofactors: implications for screening and prevention. J Natl Cancer Inst 2006;98(5):303–15.
[37] Zhao C, Weng B, Li Z, Yang H, Austin RM. Follow-up outcomes of a large cohort of low-risk women with negative imaged liquid-based cytology and negative HPV test results. Am J Clin Pathol 2013;139(1):32–8.
[38] Kulasingam SL, Havrilesky L, Ghebre R, Myers ER. Screening for cervical cancer: a decision analysis for the U.S. Preventive services task force. 2011 [Rockville MD].
[39] Pan QJ, Hu SY, Guo HQ, Zhang WH, Zhang X, Chen W, et al. Liquid-based cytology and human papillomavirus testing: a pooled analysis using the data from 13 population-based cervical cancer screening studies from China. Gynecol Oncol 2014;133(2):172–9.
[40] Katki HA, Kinney WK, Fetterman B, Lorey T, Poitras NE, Cheung L, et al. Cervical cancer risk for women undergoing concurrent testing for human papillomavirus and cervical cytology: a population-based study in routine clinical practice. Lancet Oncol 2011;12(7):663–72.